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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,817	REISBERG, BARRY	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *1-7,10,15-22,31-42,45,50-55 and 64-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-9,11-14,23-30,43-44,46-49,56-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7 April 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-66 are presented for examination.

Applicant's claim for priority under 35 U.S.C. 119(e) to United States Provisional Patent Application No. 60/411,282 filed September 17, 2002 is acknowledged. Applicant's Preliminary Amendment filed originally on April 14, 2004, and filed again on July 8, 2004 for failure to pay the fee associated with the addition of new claims in the original submission, has been received and entered into the application. Accordingly, claims 1, 4-5, 8, 23 and 34 have been amended and claims 36-66 have been newly added. Applicant's Information Disclosure Statement (IDS) filed April 7, 2004 has also been received and entered into the application. As reflected by the attached, completed copy of form PTO-1449 (one page total), the Examiner has considered the cited references.

Applicant's response to the original restriction/election requirement filed November 26, 2004 has been received and entered into the application. Applicant's response to the supplemental requirement for restriction/election filed June 20, 2005 has also been received and entered into the application.

Requirement for Restriction/Election

Applicant's response filed November 26, 2004 to the original restriction requirement dated October 26, 2004 was received by the Office. Upon further consideration of the claims by the Examiner of record, and also considering the breadth of agents presented by Applicant, a supplemental requirement for restriction/election was made on May 17, 2005. Clarifications of the supplemental requirement were further made during telephone conversations held between

the Examiner and Applicant's representative on June 7, 2005; June 13, 2005; and June 17, 2005 (see the Interview Summaries of record).

Applicant's election **with traverse** of minocycline or any tetracycline family derivative capable of crossing the blood brain barrier as the at least one first agent (i.e., the agent of Section A); the election of salicylates as the at least one second agent (i.e., an anti-inflammatory agent; the agent of Section B); the election of memantine as the at least one second agent (i.e., a glutamate induced excitotoxicity inhibitor; the agent of Section C); and the election of one agent of Section A in combination with one agent of Section B in combination with one agent of Section C in the reply filed June 20, 2005 is acknowledged.

Due to the complexity of the supplemental requirement, the supplemental requirement has been presented below in its entirety. **The requirement will not be made final at this time. A proper reply to this Office Action will include a confirmation of the groups of agents elected and the combination of agents on which Applicant wishes to pursue examination.**

The groups are set forth below.

A. Applicant is required to elect one of the following groups corresponding to the **at least one first agent**:

I. Claims 1, 23, 36 and 56, wherein the at least one first agent is minocycline or any tetracycline family derivative capable of crossing the blood brain barrier.

II. Claims 1, 23, 36 and 56, wherein the at least one first agent is acetylsalicylic acid or any salicylate which inhibits early phase cell cycle progression.

III. Claims 1, 23, 36 and 56, wherein the at least one first agent is sirolimus or any sirolimus derivative capable of inhibiting early cell cycle progression.

IV. Claims 1, 23, 36 and 56, wherein the at least one first agent is flavopiridol.

V. Claims 1, 23, 36 and 56, wherein the at least one first agent is ciclopirox.

VI. Claims 1, 23, 36 and 56, wherein the at least one first agent is a paulone.

VII. Claims 1, 23, 36 and 56, wherein the at least one first agent is indirubin.

VIII. Claims 1, 23, 36 and 56, wherein the at least one first agent is fascaplycin.

IX. Claims 1, 23, 36 and 56, wherein the at least one first agent is olomoucine.

X. Claims 1, 23, 36 and 56, wherein the at least one first agent is roscovitine.

XI. Claims 1, 23, 36 and 56, wherein the at least one first agent is Aragusterol A.

XII. Claims 1, 23, 36 and 56, wherein the at least one first agent is valproate.

XIII. Claims 1, 23, 36 and 56, wherein the at least one first agent is N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide.

XIV. Claims 1, 23, 36 and 56, wherein the at least one first agent is the farnesyl transferase inhibitor R115777.

XV. Claims 1, 23, 36 and 56, wherein the at least one first agent is the farnesyl transferase inhibitor SCH66336.

XVI. Claims 1, 23, 36 and 56, wherein the at least one first agent is the farnesyl transferase inhibitor BMS-214662.

XVII. Claims 1, 23, 36 and 56, wherein the at least one first agent is sodium butyrate.

B. Applicant is required to elect one of the following groups corresponding to the **at least one second agent (i.e., an anti-inflammatory agent)**:

XVIII. Claims 23, 36 and 56, wherein the at least one second agent is an NSAID selected from the group consisting of salicylates, ibuprofen, naproxen, celecoxib, rofecoxib, sulindac, piroxicam, indomethacin, etodolac, nabumetone, tolmetin, diclofenac, ketoprofen, apazone and meloxicam.

XIX. Claims 23, 36 and 56, wherein the at least one second agent is prednisone.

XX. Claims 23, 36 and 56, wherein the at least one second agent is cyclosporine A.

XXI. Claims 23, 36 and 56, wherein the at least one second agent is tacrolimus.

C. Applicant is required to elect one of the following groups corresponding to the **at least one second agent (i.e., an inhibitor of glutamate induced excitotoxicity)**:

XXII. Claims 28 and 61, wherein the at least one second agent is memantine.

XXIII. Claims 28 and 61, wherein the at least one second agent is neramexane.

XXIV. Claims 28 and 61, wherein the at least one second agent is amantadine.

XXV. Claims 28 and 61, wherein the at least one second agent is riluzole.

XXVI. Claims 28 and 61, wherein the at least one second agent is MK801.

XXVII. Claims 28 and 61, wherein the at least one second agent is ketamine.

XXVIII. Claims 28 and 61, wherein the at least one second agent is dextromethorphan.

XXIX. Claims 28 and 61, wherein the at least one second agent is dextrorphan.

XXX. Claims 28 and 61, wherein the at least one second agent is phencyclidine.

XXXI. Claims 28 and 61, wherein the at least one second agent is dexanabinol (HU-211).

Applicant is further required to choose one of the four possible combinations of agents, as per the telephonic conversation held between the Examiner and Ms. Mallon on June 9, 2005:

(1) One agent of Section A alone;

(2) One agent of Section A in combination with one agent of Section B;

(3) One agent of Section A in combination with one agent of Section C;

(4) One agent of Section A in combination with one agent of Section B in combination with one agent of Section C.

Claims 1-7, 10, 15-22, 31-42, 45, 50-55 and 64-66 are **withdrawn** from further consideration pursuant to 37 C.F.R. 1.142(b), as being to non-elected inventions, there being no allowable generic or linking claim. Such claims are properly withdrawn from consideration due to Applicant's election of a combination of three active agents (one agent of Section A, one agent of section B and one agent of Section C). Because this set of claims reads on the use of one agent alone (see present claim 1 or 36, for example) or a combination of two agents (see present claim 40, for example) wherein there is no option for the use of a third agent, such claims will not be examined herein because the one agent or two agent system is considered patentably distinct from a three agent system.

The claims corresponding to Applicant's election are 8-9, 11-14, 23-30, 43-44, 46-49 and 56-63 and such is the set of claims that is herein acted on the merits.

Response to Applicant's Traversal of the Present Requirement for Restriction/Election

Applicant's traversal of the present restriction requirement is on the grounds that the groups designated by the Examiner fail to define compositions and methods, with properties so distinct as to warrant separate examination and search. Applicant further submits that conjoint

examination and inclusion of all of the claims of the present application would not present an undue burden on the Examiner and, thus, requests withdrawal of the requirement.

Applicant's traversal has been carefully considered in its entirety, but does not persuade the Examiner of error in her decision to require restriction of the present set of claims. The Examiner agrees that the requirement does not set forth or properly define groups of compositions and methods. Such was not the objective of the present requirement. Given the breadth of the agents presently claimed, and also given the independent and distinct nature of each of the agents claimed, a complete search of the patent and non-patent literature for any one combination of agents would not necessarily result in a comprehensive search for any other combination of agents. Notwithstanding that Applicant may have discovered an underlying mechanism of action common to these groups of agents, such a discovery does not change the fact that each of the claimed agents lacks a common structural element as evidenced by different chemical structures and separate classification status in the art and is, thus, separately searched. In light of this, and further in light of the fact that the art does not necessarily recognize the claimed agents as sharing the common structural and common utility features as asserted by Applicant, examination of the present claims in their entirety would pose an undue burden on the Examiner.

Moreover, considering the sheer number of agents used for the therapeutic objective of treating AAMI, MCI, AD or CVD, there would exist, at minimum, 68 possible combinations of agents to be employed in this method of treatment. Such is further evidence that an undue burden would be placed on the Examiner in considering all of the combinations of agents recited in the present claims. Furthermore, even if the Examiner were to examine the complete set of claims presented by Applicant including all of the agents claimed, the *consideration of the findings* of

such a search in accordance with the requirements of the law under 35 U.S.C. §§101, 102, 103 and 112 would be unduly onerous.

For the reasons stated above, and those already made of record at pages 2-10 of the previous restriction requirement dated May 17, 2005, restriction for examination purposes is deemed proper and is grounded in the teachings of the MPEP at §800.

Applicant's Claim for Priority Under 35 U.S.C. 119(e)

The Examiner has considered the complete disclosure of the provisional application to which the present application claims benefit under 35 U.S.C. §119(e). However, the Examiner is unable to locate a teaching or fair suggestion of the presently claimed subject matter, namely the use of a three component active composition administered for the treatment of age associated memory impairment (AAMI), mild cognitive impairment (MCI), Alzheimer's Disease (AD), cerebrovascular dementia (CVD) or related retrogenic degenerative neurological conditions (see present claim 8, for example). Absent such disclosure, the application has not been afforded the benefit of the filing date of the earlier provisional application. **Accordingly, for the purposes of examination and the application of prior art, the effective filing date of the application is considered to be September 17, 2003 (the date of original filing of the instant application).**

Objection to the Specification

The disclosure is objected to because of the following minor informalities:

(i) the word "functional" is misspelled in the title of Table 1 at the top of page 8 of the disclosure; and

(ii) the word "tetracycline" is misspelled at page 19, paragraph [0048], line 3 of the disclosure.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

I Claims 9, 26, 44 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The term "derivative" in the phrase "any tetracycline family derivative capable of crossing the blood brain barrier" of present claims 9, 26, 44 and 59 is a relative term that renders the claims indefinite. In particular, "derivative" does not particularly point out the degree or type of derivation that a given compound may have in relation to the parent compound and still be considered a "derivative" as intended by Applicant. Applicant has failed to provide any specific definitions for these terms in the present specification. Lacking a clear meaning of the term "derivative", the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter for which Applicant seeks patent protection.

The MPEP sets forth the following at §2173:

> "The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention." (See MPEP §2173).

Such disclosure, however, does not render the claims definite. Words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art

unless defined by Applicant in the specification with "reasonable clarity, deliberateness and precision" (MPEP §2111.01). Here, the disclosure lacks a definition for the term "derivative" does not set forth in a reasonably clear, deliberate or precise manner what other compounds may be considered tetracycline family derivatives. That is, there is no **limiting** definition provided for this term. Thus, the identity of those compounds that are included or excluded by the phrase "any tetracycline family derivative capable of crossing the blood brain barrier" is open to subjective interpretation and such is inconsistent with the tenor and express requirements of 35 U.S.C. §112, second paragraph.

II Claims 8-9, 11-14, 43-44 and 46-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The phrase "related retrogenic degenerative neurological conditions" of present claims 8-9, 11-14, 43-44 and 46-49 is a phrase that renders the claims indefinite. In particular, the presently claimed subject matter and corresponding disclosure does not particularly point out the degree or type of relationship that a given retrogenic degenerative condition may have to those that are presently claimed (i.e., AAMI, MCI, CVD or AD) and still be considered a "retrogenic degenerative neurological condition" as intended by Applicant. Furthermore, Applicant has failed to provide any specific definition for this phrase in the present specification. Lacking a clear meaning of such a phrase, the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter for which Applicant seeks patent protection.

Applicant sets forth the following at page 7, paragraph [0023]:

"By the term 'related retrogenic diseases"...and the like, is meant neurological conditions

> that present some degree of degeneration from the normal adult neurological condition. This includes measurable decline of normal cognitive, neurologic, or functional capacity."

Such disclosure, however, does not render the claims definite. Words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art unless defined by Applicant in the specification with "reasonable clarity, deliberateness and precision" (MPEP §2111.01). Here, the disclosure lacks a definition for the term "related retrogenic degenerative neurological conditions" does not set forth in a reasonably clear, deliberate or precise manner what other diseases would be considered retrogenic degenerative neurological conditions and how one skilled in the art would determine whether such a condition was properly characterized as a retrogenic degenerative neurological condition through measurement of cognitive and/or overall function. There is no **limiting** definition provided for this phrase. Thus, the identity of those disease states that are included or excluded by the phrase "related retrogenic degenerative neurological conditions" is open to subjective interpretation and such is inconsistent with the tenor and express requirements of 35 U.S.C. §112, second paragraph.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-9, 11, 13, 43-44, 46, 48, 56-60 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Duncan (WO 02/020022 A1; March, 2002).

Duncan teaches the administration of a tetracycline compound, such as minocycline, doxycycline or any tetracycline compound of the formula (I) (page 2, line 25-page 3, line 6), in an effective amount for the treatment of neurologic disorders, such as Alzheimer's disease, in an effective amount sufficient to down regulate microglia expression, activation and production (page 2, lines 9-24 and see also Example 1). Duncan further teaches that the tetracycline compound may be administered with an agent capable of inhibiting inflammation in tissue, e.g., steroidal or non-steroidal anti-inflammatory drugs (page 6, lines 3-16).

The Examiner has noted that present claims 8 and 43 require at least one first agent capable of inhibiting neuronal cell cycle progression at or before an early phase, at least one second agent capable of inhibiting neuronal cell cycle progression generally and optionally at least one third agent capable of inhibiting mitogenic stimulation. However, absent express disclosure by Applicant stating that the at least one first agent cannot be the same as the at least one second agent, the Examiner considers the use of minocycline or a tetracycline compound as taught by Duncan to meet both the limitation of (i) at least one first agent capable of inhibiting neuronal cell cycle progression at or before an early phase and (ii) at least one second agent capable of inhibiting neuronal cell cycle progression.

Regardless of whether minocycline or a tetracycline compound inhibits neuronal cell cycle progression selectively at or before an early phase or simply "generally" as Applicant has stated in claims 8 and 43, the therapeutic endpoint is still the same, i.e., the inhibition of neuronal cell cycle progression, irrespective of what point in the cell cycle the compound actually inhibits progression. Such is further support that the at least one first agent and the at least one second

agent are not required to be distinct from one another. Thus, for the purposes of examination, the Examiner has interpreted the limitations at least one first agent and the at least one second agent to be met by Duncan, who discloses the use of minocycline or a tetracycline compound.

Furthermore, while the Examiner had noted the recitation of the limitation "wherein the at least one first agent inhibits cell cycle progression...and/or reducing activated microglia-induced mitogenic stimulation" in present claim 57 (see lines 1-4) and the limitation "wherein the at least one first agent inhibits cell cycle progression at or prior to entry of a neuronal cell...and/or reducing activated microglia-induced mitogenic stimulation" in present claim 58 (see lines 1-4), such limitations are considered a functional limitation of the agents and, thus, fail to further limit the claimed method. Nevertheless, because the claimed active agents are also taught by the prior art of Duncan for the same therapeutic purposes, there is no reason to doubt that the agents of the patent publication do not selectively act on cells in the S or G1 phase or that they are capable of inhibiting glutamate-induced excitotoxicity and/or reducing activated microglia-induced mitogenic stimulation, absent factual evidence to the contrary. Applicant's attention is further drawn to the MPEP at §2113, which states, "As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Lastly, the Examiner notes that while Alzheimer's disease is not expressly recited in present claim 8, absent factual evidence to the contrary, and absent any limiting definition provided by Applicant (see above, under "Claim Rejections-35 U.S.C. 112, Second Paragraph"), the Examiner considers such a condition to meet Applicant's limitation of a "related retrogenic degenerative neurological condition" (see present claim 8, line 1).

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-9, 11-14, 23-30, 43-44, 46-49 and 56-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan as applied to claims 8-9, 11, 13, 43-44, 46, 48, 56-60 and 62 for the reasons made of record above, and further in view of Lipton (WO 92/17168; 1992), Lee et al. (U.S. Patent No. 6,043,224; 2000) and Gervais et al. (U.S. Patent Application Publication 2005/0031651; 2005, priority to U.S. Provisional Application 60/482,214 filed June, 2003).

The differences between the Duncan reference and the presently claimed subject matter lie in that the reference does not teach:

(i) the use of memantine and an inhibitor of glutamate-induced excitotoxicity;

(ii) the use of salicylates as the anti-inflammatory agent; and

(iii) the treatment of age-associated memory impairment, mild cognitive impairment, or cerebrovascular dementia.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) It is acknowledged that Duncan is silent as to the use of the disclosed composition (i.e., comprising minocycline (or a tetracycline compound) and an anti-inflammatory agent) in further combination with memantine, an inhibitor of glutamate-induced excitotoxicity. However, it was well known in the art that memantine was useful for the same therapeutic purpose of treating Alzheimer's disease by reducing neuronal damage by blocking NMDA receptor-operated channel activation by excitatory amino acids, such as glutamate-related compounds, when administered in an amount sufficient to block glutamate's effect on the NMDA receptor (see Lipton, et al., page 4, lines 23-31, page 10, lines 14-17 and page 10, line 32-page 11, line 3). It would, therefore, have been obvious to a person of ordinary skill in the art to employ memantine in combination with the composition disclosed by Duncan because each was known in the art to be successful for achieving the same therapeutic effect. Motivation to administer both compounds flows logically from the efficacy of each compound in treating Alzheimer's disease and other neurodegenerative diseases as demonstrated in the prior art and also because each compound has been previously administered for the same therapeutic endpoints. In the absence of evidence to the contrary, it is generally *prima facie* obvious to use in combination two or more agents that have previously been used separately for the same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA).

(ii) Although Duncan broadly teaches the use of anti-inflammatory agents, both steroidal and non-steroidal, in combination with minocycline or a tetracycline compound, the reference is silent as to the particular use of salicylates as the anti-inflammatory compound. However, the use of salicylates in compositions effective for the treatment of neurodegenerative diseases, such as Alzheimer's disease, was well known in the art at the time of the invention. Lee et al. teaches compositions of non-steroidal anti-inflammatory agents, such as aspirin or salicylic acid or the

salicylates Asacol, Disalcid, Pentesa, Salflex or Trilisate, for the treatment of Alzheimer's disease and other neurodegenerative diseases (col.5, lines 10-16; col.10, lines 38-42 and col.18, lines 25-58). It would, therefore, have been obvious to a person of ordinary skill in the art to employ any one or more of these known salicylate-type non-steroidal anti-inflammatory agents in the composition disclosed by Duncan because each would have been reasonably expected to exert the same inflammation-reducing effects as those required by the reference.

(iii) Although the previously cited references are silent as to the treatment of conditions such as age-associated memory impairment, mild cognitive impairment or cerebrovascular dementia, such conditions were known in the art to be related to the peptide amyloid-β, as taught by Gervais et al. (U.S. Patent Application Publication 2005/0031651; page 3, paragraph [0024]). In light of the fact that Duncan expressly teaches the minocycline (or a tetracycline compound)/anti-inflammatory composition useful for the treatment of Alzheimer's disease, which he expressly states is characterized by amyloid plaques associated with upregulated microglial cell expression (see page 1, line 28-page 2, line 2 and 23-24) and that memantine is also useful for the same therapeutic objective of treating Alzheimer's disease, it would have been appreciated by the skilled artisan that such a combination of agents would have been useful in the treatment of other disorders associated with the amyloid peptide, such as age-associated memory impairment (considered by the Examiner to be synonymous with age-related cognitive decline), mild cognitive impairment or cerebrovascular dementia. Such a person would have been motivated to treat such conditions with this combination of agents because it would have been reasonably expected that such a combination would demonstrate the same or a similar level of efficacy against other amyloid peptide related diseases as it would against the treatment of Alzheimer's disease.

Moreover, age-associated memory impairment and mild cognitive impairment are further considered by the Examiner to be progressive conditions that precede the development of mature Alzheimer's disease. Thus, because such a combination would have efficacy in treating the advanced condition of Alzheimer's disease, it would also be reasonably expected that the same combination of agents would have efficacy in treating the less severe conditions directly associated to and preceding the development of advanced Alzheimer's.

Conclusion

Rejection of claims 8-9, 11-14, 23-30, 43-44, 46-49 and 56-63 is deemed proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leslie A. Royds
Patent Examiner
Art Unit 1614

July 7, 2005

RAYMOND HENLEY III
PRIMARY EXAMINER
AU 1614